UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/603,208	06/23/2000	Markus Pompejus	BGI-124CP	9692

959 7590 11/06/2002

LAHIVE & COCKFIELD
28 STATE STREET
BOSTON, MA 02109

EXAMINER
SPIEGLER, ALEXANDER H

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 11/06/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

File

Office Action Summary	Application No.	Applicant(s)	
	09/603,208	POMPEJUS ET AL.	
	Examiner	Art Unit	
	Alexander H. Spiegler	1637	

-- The MAILING DATE of this communication appears on the cover she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 July 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *40 and 42* is/are allowed.

6)☒ Claim(s) *39,41 and 43-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to Paper No. 10, filed on July 8th, 2002. Currently, claims 39-70 are pending, claims 1-38 having been canceled. All arguments have been fully considered and thoroughly reviewed, but are deemed not persuasive for the reasons that follow. This action is made FINAL. Any objections and rejections not reiterated below are hereby withdrawn. Specifically, the 102 and 103 rejections have been withdrawn due to Applicants' amendment to the claims.

Specification

2. The disclosure is objected to because of the following informalities:

A) Tables 1-4 are not in the specification. Applicants should send the postcard receipt which shows that Tables 1-4 were received from the Patent Office, as well as, another copy of Tables 1-4. Additionally, Applicants must note where the Tables 1-4 should be inserted in the specification.

Appropriate correction is required.

THE FOLLOWING ARE NEW GROUNDS OF REJECTION NECESSITATED BY APPLICANTS AMENDMENTS TO THE CLAIMS

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 69-70 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claim 69 is indefinite over "the regulatory region" and "the wild-type regulatory region" because these recitations lack antecedent basis.

B) Claim 70 is indefinite over "sufficiently identical" because it is not clear as to what this recitation means, and this recitation is not defined in the specification.

First Paragraph-Written Description

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 39, 41 and 43-70 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to an isolated nucleic acid comprising SEQ ID NO: 1, nucleic acids encoding a polypeptide comprising SEQ ID NO: 2, nucleic acid, a nucleotide sequence which is at least 70, 80 or 90% identical to SEQ ID NO:1, a nucleic acid molecule encoding a polypeptide fragment comprising at least 100 contiguous amino acids, a nucleic acid molecule encoding a polypeptide comprising an amino acid at least 70, 80 or 90% identical to SEQ ID NO: 2.

It is not clear whether SEQ ID NO: 1 is a full-length cDNA, encoding a full-length protein. The instant specification only describes the isolated nucleic acid from *Corynebacterium glutamicum* consisting of instantly claimed SEQ ID NO: 1. The specification further teaches that SEQ ID NO: 1 is a gene consisting of 1566 bp. In light of the open claim language used (see

above), these claims encompass any full length sequence in which the instantly recited nucleic acids may be embedded, for example the full length genes. Therefore, it has been interpreted that the claims are inclusive of genomic sequences, including intron sequences and regulatory sequences, in addition to the full-length cDNA sequence. Furthermore, the claims include language so as to include variants of the disclosed sequences, and any sequence which hybridizes to the disclosed sequences. Claim 52 is inclusive of sequences from other species, mutated sequences, allelic variants with functional activities distinct from that of SEQ ID NO:1, and a large genus of nucleic acids not described in the specification. However, none of these additional sequences meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed* (See page 1117)." The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed (See Vas-Cath at page 1116)."

With the exception of SEQ ID NO: 1, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606

(CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

It is noted that in Fiers v. Revel (25 USPQ2d, 1601), the Fed. Cir. concluded that "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."
In the instant application, only the nucleic acid consisting of instant SEQ ID NO: 1 is described.

In the application at the time of filing, there is no record or description which would demonstrate conception or written description of a isolated nucleic acid comprising SEQ ID NO: 1, nucleic acids encoding a polypeptide comprising SEQ ID NO: 2, nucleic acid, a nucleotide sequence which is at least 70, 80 or 90% identical to SEQ ID NO:1, a nucleic acid molecule encoding a polypeptide fragment comprising at least 100 contiguous amino acids, a nucleic acid molecule encoding a polypeptide comprising an amino acid at least 70, 80 or 90% identical to SEQ ID NO: 2. Therefore, only the nucleic acid consisting of SEQ ID NO: 1, but not the full breadth of the claim meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant.

Furthermore, it is also noted that Applicants were not in possession of nucleic acids that encode polypeptides, which are "capable of resistance to a chemical stress" or "capable of

modulating the production of a fine chemical". Applicants provide not examples or evidence that they were in possession nucleic acids that encode polypeptides, which are "capable of resistance to a chemical stress" or "capable of modulating the production of a fine chemical"

If Applicants traverse this rejection, Applicants should explicitly point to where in the specification there is support for the evidence that SEQ ID NO: 1 is a full-length cDNA sequence. Furthermore, if, and once this is established, Applicants should amend the claims that recite % identity to include functional language. Furthermore, claim 52 should be amended to "consisting of at least 100 contiguous amino acids".

Applicants Arguments

Applicants argue that variants of a polypeptide (i.e. polypeptides that are 70, 80 or 90% identical) to a polypeptide would fall within the written description guidelines if they are supported with functional language, and that the instant claims are drawn to nucleic acids encoding polypeptides with functional language.

Response to Applicants Arguments

Applicants arguments have been considered, but are not persuasive for the following reasons.

Applicants are correct to identify variants of a polypeptide (i.e. polypeptides that are 70, 80 or 90% identical) to a polypeptide would fall within the written description guidelines if they are supported with functionally language (see pg. 11 of Applicants response). Applicants contest that the variants of the polypeptide, SEQ ID NO: 2, are "capable of resistance to a chemical stress" or "capable of modulating the production of a fine chemical" (pg. 12). However, Applicants were not in possession of nucleic acids encoding polypeptides having these functions,

as the specification does not provide any examples, evidence or reason to arrive at Applicants' contentions.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claim 43-68 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid from *Corynebacterium glutamicum* consisting of instantly claimed SEQ ID NO: 1 (and an insolated nucleic acid encoding SEQ ID NO: 2), does not reasonably provide enablement for an isolated nucleic acid from *Corynebacterium glutamicum* nucleic acids that at least 70, 80 or 90% identical to SEQ ID NO: 1 which encodes a polypeptide, nucleic acids encoding polypeptides that are at least 70, 80 or 90% identical to SEQ ID NO: 2, or a nucleic acid molecule encoding a polypeptide fragment comprising at least 100 contiguous amino acids, wherein the polypeptides are either "capable of resistance to a chemical stress" or "capable of modulating the production of a fine chemical". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 43-68 are broadly drawn to nucleic acids that at least 70, 80 or 90% identical to SEQ ID NO: 1, or nucleic acids encoding polypeptides that are at least 70, 80 or 90% identical to SEQ ID NO: 2, or a nucleic acid molecule encoding a polypeptide fragment comprising at least 100 contiguous amino acids.

The specification does not enable one of ordinary skill in the art to practice the invention as broadly claimed for the following reasons:

The instant specification teaches the isolated nucleic acid from *Corynebacterium glutamicum* consisting of instantly claimed SEQ ID NO: 1. The specification further teaches that SEQ ID NO: 1 is a gene consisting of 1566 bp.

Case law has established that "(t)o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" In re Wright 990 F.2d 1557, 1561. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) it was determined that "(t)he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art". The amount of guidance needed to enable the invention is related to the amount of knowledge in the art as well as the predictability in the art. Furthermore, the court in Genetech Inc. v Novo Nordisk 42 USPQ2d 1001 held that "(I)t is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of the invention in order to constitute adequate enablement".

In the instant case, the claims are not commensurate in scope with the enabling disclosure because the claims are drawn to fragments of nucleic acids encoding polypeptides "capable of resistance to a chemical stress" or "capable of modulating the production of a fine chemical". The specification provides no examples or evidence that the nucleic acids encode polypeptides "capable of resistance to a chemical stress" or "capable of modulating the production of a fine chemical". These alleged functions of the encoded polypeptides are not enabled, as the specification does not teach any examples demonstrating these alleged functions. Furthermore, even assuming the specification did teach an example that demonstrated one of these functions (which it does not), the recitation of "capable of resistance to a chemical stress" or "capable of

modulating the production of a fine chemical" is an extremely broad in terms of defining a function of a polypeptide. As evidenced by the specification, there are a plurality of possible "fine chemicals" (page 8) and "chemical stresses" (pages 15-16) that are distinct and unrelated. In other words, while a nucleic acid may encode a polypeptide "capable of modulating the production" a nucleotide (e.g. fine chemical), it may not encode a polypeptide "capable of modulating the production" a lipid (e.g. fine chemical). Applicants have neither taught one nucleic acid encoding a polypeptide "capable of the modulation" of one fine chemical, let alone a nucleic acid encoding a polypeptide that could enable "modulation" of any possible fine chemical or any possible "chemical stress". To obtain the claimed nucleic acids, one of skill in the art would have to perform labor-intensive experiments to find nucleic acids that encode polypeptides that are "capable of resistance to [any] chemical stress" or "capable of modulating the production of [any] fine chemical". These experiments are not only labor-intensive, but are highly unpredictable, given the lack of guidance in the specification.

In view of the high level of unpredictability in the art and in view of the lack of specific disclosure in the specification regarding the make and use of the substantially large number of possible sequences encompassed by the claims, undue experimentation would be required to practice the invention as it is broadly claimed.

Applicants Arguments

Applicants argue that the specification teaches one of ordinary skill in the art how to make and use claimed nucleic acids, and that any experimentation to make the claimed nucleic acids would be routine.

Response to Applicants Arguments

Applicants arguments have been considered, but are not persuasive for the following reasons.

While the specification may teach general methods for making nucleic acids and expressing polypeptides, the specification does not teach experiments of making and using nucleic acids which encode polypeptides that are "capable of resistance to [any] chemical stress" or "capable of modulating the production of [any] fine chemical". Even assuming that the specification did teach general methods for making and using these nucleic acids, the experimentation required of one skilled in the art would be undue, as the claims are broadly drawn to nucleic acids encoding polypeptides that are "capable of resistance to [any] chemical stress" or "capable of modulating the production of [any] fine chemical". This class of nucleic acids is very large, which would result in a very labor-intensive and time-consuming experimentation process for one skilled in the art.

Conclusion

9. The prior art does not teach or suggest the isolated nucleic acid sequence from *Corynebacterium glutamicum* consisting of SEQ ID NO: 1, which encodes SEQ ID NO: 2.

10. Claims 40 and 42 are allowable.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (703) 305-0806. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014. Applicant is also invited to contact the TC 1600 Customer Service Hotline at (703) 308-0198.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Alexander H. Spiegler
November 1, 2002

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

11/4/02